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Spinal muscular atrophy drug may help kids with later-onset disease

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There is now further evidence that a drug that is effective in treating the rare muscle-wasting disease spinal muscular atrophy (SMA) early in life may be associated with improvement in older children, according to a study published in the April 24, 2019, online issue of *Neurology*, the medical journal of the American Academy of Neurology.

Spinal muscular atrophy is a neurodegenerative disease that attacks nerve cells in the spinal cord, leading to muscle weakness. This can affect breathing, swallowing, walking and head control. There are several types of SMA, some of them fatal. SMA type I is the most common and most severe form of the disease. It starts before the age of six months, with infants never gaining the ability to sit up. The median survival rate is eight to 14 months old.

In babies with SMA type II, symptoms start after six months; they reach the ability to sit and some may be able to stand with support but they are unable to walk. In SMA type III, symptoms start after children are 18 months old; they are able to walk but become progressively weaker and some lose the ability to walk over time.

"This study involved kids up to age 15 years at enrollment with SMA types II and III, and they were followed for approximately three years, so we were excited to see that the drug can show benefit for these older kids too and that the benefit can extend for this period of time," said study author Basil T. Darras, MD, of Boston Children's Hospital and Harvard Medical School and a member of the American Academy of

Neurology.

For the study, 28 children with spinal muscular atrophy—11 with type II and 17 with type III—received injections of the drug nusinersen into the spinal canal two to three times over 85 days and then were followed for an additional six months. The drug is the first and only approved treatment for all types of SMA. It works by increasing the production of a certain protein that is essential for motor neurons in the spinal cord to survive. The phase 1/2a study was open-label, which means that both the researchers and the participants and their families were aware of the drug that they were given.

After that part of the study ended, 24 of the children continued on and received four doses of the drug six months apart in an extension study.

Participants' movement abilities were tested at the beginning of the study, during the study and again six months after the last drug treatment.

"The children's motor function improved, and their disease activity stabilized in ways that were definitely not consistent with the normal history of this disease," Darras said. "One of the children with SMA type II gained the ability to walk independently after about 18 months of treatment and continued to improve during the study. Two of the four children with SMA type III who had lost the ability to walk before the study started regained their ability to walk independently."

In a test of how well participants could perform skills such as sitting without support, rolling onto their side, kneeling, or standing with or without support, the children with SMA type II improved by an average of 10.8 points, where an individual improvement of at least three points was considered meaningful and normally kids with this type of SMA would decline by an average of 1.7 points during the same time period.

On a test of how many meters they could walk in six minutes, the children with SMA type III who were able to walk at the beginning of the study improved by an average of 36 meters a year after starting the treatment, where an individual improvement of at least 30 meters was considered meaningful and normally kids with this type of SMA would decline by an average of 1.5 meters during the same time period. The five children who completed this test at the end of the study improved by an average of 92 meters.

None of the children stopped taking the drug due to side effects.

Limitations of the study included the small number of participants, the open-label design where participants, families and researchers all knew what treatment they were receiving and the lack of control groups within the study. The results do not prove cause and effect between the treatment and the improvements; they only show an association.

Provided by American Academy of Neurology